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CLAIMS :

- 1 - Mucopolysaccharide fraction obtainable from heparin or from fractions including heparinic constituents of molecular weights from 2.000 to 50.000, this fraction being characterized in that it is soluble in an aqueous-alcoholic medium (water-ethanol) having a titer of 55-61° GL, in that it tends to insolubility in a water-ethanol medium having a higher alcohol content, in that it is insoluble in pure alcohol, and in that it has a Yin-Wessler titer and a USP titer which are respectively in a ratio at least equal to 2, notably at least 3, preferably higher than 6.
- 2 - Mucopolysaccharide fraction according to claim 1, characterized in that the ratio of its Yin-Wessler titer to its USP titer is higher than 10, even than 16.
- 3 - Mucopolysaccharide fraction according to claim 1 or claim 2, characterized in that it is essentially formed from constituents whose molecular weights are less than 10 000 .
- 4 - Mucopolysaccharide fraction according to claim 3, characterized in that it is essentially formed of constituents whose molecular weights are comprised between about 2 000 and about 8 000 .
- 5 - Mucopolysaccharide fraction according to any one of claims 1 to 4, characterized in that, in a gel-

filtration operation on a column of gel of polyacrylamide and of agarose, in bead form, of the type marketed under the name ULTROGEL ACA 44, it is obtained in the 1.5 litres of eluate which follow the elution of a volume of 2.5 litres, dead volume not included, when the gel-filtration is conducted, at a flow rate of 200 ml/hour, on a column having a diameter of 100 mm and a height of 1 m and when the concentration of mucopolysaccharide and the volume of the solution placed on the column have been respectively 50 mg/ml and 37.5 ml.

6 - Mucopolysaccharide fraction according to any one of claims 1 to 5, characterized in that it is constituted by the fraction which, in a gel-permeation system on columns filled with silica with a granulometry of 10 to 100 microns, of 250 mm height and 9 mm diameter, is characterized by a retention time of the order of 5.7 to 7.5, notably from 6.6 to 7.0 minutes in such column, when 50 μ l of a solution of 1.3 mg/ml of this fraction in a 0.02 M Na_2SO_4 buffer, are placed on this column and then eluted at a flow rate of 3 ml/minute.

7 - Mucopolysaccharide fraction according to any one of claims 1 to 6, characterized by ratios of Yin-Wessler/USP titers exceeding 10, notably of the order of 13-16, and having Yin-Wessler titers higher than 130, notably from 135-160 units/mg.

8 - Mucopolysaccharide fraction characterized in that
- it is soluble in an aqueous-alcoholic medium

(water-ethanol) having a titer of 55-61 GL ;

- it tends to insolubility in a water-ethanol medium having a higher alcohol content, and it is insoluble in pure alcohol;

- it has a Yin-Wessler titer higher than 130 units/mg ;

- its Yin-Wessler titer and its USP titer are respectively in a ratio above 13;

- it is essentially formed from constituents whose molecular weights are less than 10 000; particularly between about 2 000 and about 8 000;

- in a gel-filtration operation on a column of gel of polyacrylamide and of agarose, in bead form, of the type marketed under the name ULTROGEL Aca 44, it is obtained in the 1.5 litres of eluate which follow the elution of a volume of 2.5 litres, dead volume not included, when the gel-filtration is conducted, at a flow rate of 200 ml/hour, on a column having a diameter of 100 mm and a height of 1 m and when the concentration of mucopolysaccharide and the volume of the solution placed on the column have been respectively 50 mg/ml and 37.5 ml;

- in a gel-permeation system on columns filled with silica with a granulometry of 10 to 100 microns, of 250 mm height and 9 mm diameter, said fraction is characterized by a retention time of the order of 5.7 to 7.5, notably from 6.6 to 7.0 minutes in such column, when 50 μ l of a solution of 1.3 mg/ml of this fraction in a 0.02 M Na₂SO₄ buffer, were placed on this column, and then eluted at a flow rate of 3 ml/minute.

9 - Mucopolysaccharide fraction according to claim 8 characterized by a ratio of Yin-Wessler/ USP titers of the order of 13-16, and a Yin-Wessler titer from 135-160 units/mg.

10 - Mucopolysaccharide fraction according to anyone of claims 1 to 9 characterized by its capability of being fixed by Antithrombin III.

11 - Mucopolysaccharide fraction according to claim 10, characterized by its capacity to be fixed on an antithrombin III fixed to a support, such as agarose, in an 0.2 M NaCl, 0.05 M tris-HCl buffer at pH 7.5 and by Yin-Wessler and USP titers which are in a ratio (YW/USP ratio) at least equal to 6, the Yin-Wessler titer itself being at least equal to 300 U/mg.

12 - Fraction according to claim 10 or 11, characterized by a YW/USP ratio higher than 18 and a Yin-Wessler activity higher than 900 U/mg.

13 - Fraction according to anyone of claims 10 to 12, characterized by a YW/USP ratio higher than 50.

14 - Fraction according to claim 13 characterized by a YW/USP ratio higher than 65 with a Yin-Wessler activity higher than 1 300 U/mg.

15 - Fraction or compound according to anyone of claims 10 to 14, characterized by an NMR spectrum for the

(¹H) proton, effected on a solution of this compound dissolved in deuteriated water at 35°C with a radiation of 270 megahertz, which comprises, as characteristic elements of the spectrum, resonance signals which, for chemical displacements of the order of 4.8 and 5.2 ppm, are substantially weaker than the resonance signal which is also observed for a chemical displacement of the order of 5.4 ppm (reference for the measurement of the displacements: sodium 3-trimethylsilyl propionate 2.2, 3.3-d₄).

16- Fraction or compound according to anyone of claims 10 to 15, characterized by an NMR spectrum for carbon 13 (¹³C), carried out on a solution of this compound dissolved in deuteriated water with a radiation of 20 MHz, which comprises, as characteristic elements of the spectrum (reference for the measurement of the displacements: tetramethylsilane) :

- the practical absence of resonance signals characteristic of the presence of OH groups on the primary carbon (in the 6 position) of the glucosamine units contained in said mucopolysaccharide fraction,
- supplementary signals, in the region of the (I₁) and (G₁) signals, in regions corresponding to the chemical displacements of the order of 100 ppm,
- a supplementary signal (G₂) close to the N-sulphated G₂ signal in the 60 ppm region,
- the presence of a resonance signal in the 75 ppm region.

17 - Fraction or compound according to anyone of

claims 10 to 16, characterized by an NMR spectrum in conformity with that of one at least of Figures 11, 12, 14 and 15.

18 - Fraction or compound according to claim 17, characterized in that it is formed by a homogeneous oligosaccharide having also the following additional characteristics:

- it comprises from 8 to 12, notably 10 monosaccharide units;
- all the primary positions of the glucosamine units of this oligosaccharide are sulphated;
- this oligosaccharide includes one N-acetylglucosamine unit per two units of 2-O-sulphate iduronic acid and per two N-sulphate-glucosamine units, the other saccharides being of a different nature and including distinct substituents.

19 - Fraction of compound according to claim 18, characterized by a molecular weight of about 2 000 to about 3 000, notably of about 2 500 .

20 - Fraction or compound formed by a homogeneous oligosaccharide having also the following additional characteristics;

- it comprises from 8 to 12, notably 10 monosaccharide units;
- all the primary positions of the glucosamine units of this oligosaccharide are sulphated;

- this oligosaccharide includes one N-acetyl-glucosamine unit per two units of 2-O-sulphate iduronic acid and per two N-sulphate-glucosamine units, the other saccharides being of a different nature and including distinct substituents;

- it exerts selective inhibition of the Xa factor in vitro and in vivo;

- it fixes on Antithrombin III.

21 - Fraction or compound according to claim 20, characterized by an NMR spectrum for the (^1H) proton, effected on a solution of this compound dissolved in deuteriated water at 35°C with a radiation of 270 megahertz, which comprises, as characteristic elements of the spectrum, resonance signals which, for chemical displacements of the order of 4.8 and 5.2 ppm, are substantially weaker than the resonance signal which is also observed for a chemical displacement of the order of 5.4 ppm (reference for the measurement of the displacements: sodium 3-trimethylsilyl propionate 2,2, 3,3- d_4).

22 - Fraction or compound according to claim 20 or 21, characterized by an NMR spectrum for carbon 13 (^{13}C), carried out on a solution of this compound dissolved in deuteriated water with a radiation of 20 MHz, which comprises, as characteristic elements of the spectrum (reference for the measurement of the displacements: (tetramethylsilane) :

- the practical absence of resonance signals characteristic of the presence of OH groups on the primary carbon (in the 6 position) of the glucosamine units contained in said mucopolysaccharide fraction,

- supplementary signals, in the region of the (G₁) and (G₂) signals, in regions corresponding to the chemical displacements of the order of 100 ppm,

- a supplementary signal (G₂) close to the N-sulphated G₂ signal in the 60 ppm region,

- the presence of a resonance signal in the 75 ppm region.

23 - Fraction or compound according to anyone of claims 20 to 22 characterized by a molecular weight of from about 2 000 to 3 000, notably of about 2 500.

24 - Monopolysaccharide fraction according to any one of claims 1 to 23, characterized in that its constituents are in the state of salts of at least one physiologically acceptable metal, such as sodium or calcium.

25 - Process for preparing a mucopolysaccharide fraction having a high Yin Wessler titer and a low USP titer, characterized by:

- suspending in an aqueous-alcoholic medium of the water-ethanol type, having a titer comprised between about 55 and about 61° GL, preferably of the order of 58° GL, a substance based on heparin or heparinic constituents whose molecular weights range notably from 2 000 to 50 000, this substance having a reduced content

of inorganic salts, preferably less than 1 % by weight,

- separating the insoluble fraction and recovering the ~~solution~~ containing the dissolved mucopolysaccharide fraction, from which it can in its turn be separated, notably by alcoholic precipitation.

25 - Process according to claim 25 which comprises subjecting an aqueous solution of the fraction obtained by the process of claim 24 to gel-filtration under conditions so adjusted as to enable fractions which possess even higher Yin-Wessler/USP titer ratios to be obtained.

27 - Process according to claim 25 or 26 which comprises producing further such enrichment by contacting any of the preceding fractions with immobilized antithrombin III to produce selective fixation thereon of the most active fractions in terms of Yin-Wessler activity and recovering the latter by elution with a buffer capable of producing desorption.

28 - Pharmaceutical composition containing the mucopolysaccharide fraction according to anyone of claims 1 to 24 in association with a pharmaceutically acceptable vehicle.

29 - Composition according to claim 28 in dosage unit form characterized in that it is in the form of a sterile injectable concentrated solution of this fraction, usable in therapeutics for the control of blood coagulation,

which solution contains from 1 000 to 100 000 U (Yin-Wessler)/ml of the mucopolysaccharide fraction, preferably from 1 000 to 50 000, for example 25 000 U/ml, when these solutions are intended for sub-cutaneous injection, or containing again, for example from 500 to 10 000, for example 5 000 U/ml of the mucopolysaccharide fraction, when it is intended for intravenous injection or for perfusion.